CLEFT PALATE ONLY: CURRENT CONCEPTS

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SUMMARY
Cleft palate only (CPO) is one of the most common congenital malformations worldwide. The etiopathogenesis of CPO is not completely understood. Environmental factors, such as smoking, alcohol consumption, intake of drugs during pregnancy, advanced paternal age, have been demonstrated to be a risk of CPO, but conflicting results have also been published. Insufficient intake of folic acid during the pregnancy has been suggested to increase the risk for CPO. The demonstrated risk for siblings and the higher risk for monozygotic twins suggest a genetic etiopathogenesis for CPO. In some cases of CPO a prevalent mode of inheritance has been reported, but oligogenic models with reduced penetrance, and the risk related to environmental factors have also been proved. One of the first manifestations associated with CPO is difficulty with feeding. Aerophagia is a problem in these infants with CPO and requires more frequent burping and slower feeding. The inability to generate intraoral breath pressure due to nasal air emission in CPO children frequently manifests as articulation difficulties, particularly consonant weakness, and unintelligible speech. Hearing disorders are prevalent among individuals with CPO, as a result of chronic otitis media with effusion due to eustachian tube dysfunction. A multidisciplinary team is essential to manage the many aspects of CPO. In treating CPO, the reconstructive surgeon works in cooperation with otolaryngologists, dentists and orthodontists, speech pathologists, audiologists, geneticists, psychiatrists, maxillofacial surgeons, social workers, and prosthodontists. CPO can be considered a genetically complex disease, but new knowledge and new therapeutic approaches have greatly improved the quality of life of these children. Prenatal diagnosis is an important step in the treatment of this disease.

Key words: congenital, cleft palate, cleft palate only, birth defects, genetic epidemiology.

Introduction

Cleft palate only (CPO) is one of the most common congenital malformations worldwide. CPO can be non-syndromic or it can appear as a part of a syndrome or recurrence pattern. Non-syndromic cleft palate (NSCF) and non-syndromic cleft lip (NSCL) with or without cleft palate (CL/P) are considered different pathologies on the basis of embryology and epidemiology. Despite this knowledge, CPO may segregate in the same pedigree, suggesting that they might share a common genetic background. Oral clefts manifest in hundreds different syndromes, and in some of these the gene defect is already known. Studies on mutations in NSCF have reported that distinct types of genes may influences different syndromes. It has been established that the half of cases of CPO are non-syndromic. The etiopathogenesis of CPO is not completely understood. Environmental factors, such as smoking, alcohol consumption, intake of drugs during pregnancy, advanced paternal age, have been demonstrated to be a risk of CPO, but conflicting results have also been published. Insufficient intake of folic acid during the pregnancy has been suggested to increase the risk for CPO. The demonstrated risk for siblings and the higher risk for monozygotic twins suggest a genetic etiopathogenesis for CPO. In some cases of CPO a prevalent mode of inheritance has been reported, but oligogenic models with reduced pene-

trance, and the risk related to environmental factors have also been proved. The risk of developing CPO is related to its presence in parents or siblings (2% if one sibling with CPO, 6% if one parent with CPO, and 15% if one sibling and one parent with CPO). Finally it is debated if CPO is a multifactorial syndrome with a strong genetic background combined with environmental factors (1).
CPO is one of the most common congenital cranio-facial anomalies evaluated by a surgeon. CPO is being detected earlier, often with fetal ultrasound and magnetic resonance imaging (MRI), thus preparing parents with a prenatal diagnosis. The pregnant woman is usually visited by a surgeon before to the birth of her child. Successful treatment of CPO depends on accurate pre-natal evaluations, surgical experience, knowledge of three-dimensional (3D) normal and abnormal anatomy, detailed postoperative and longitudinal care, and collaboration with a multidisciplinary team. The consequences of CPO are not limited to cosmetic deformities, but also to dental abnormalities, speech distortion, disorganized swallowing, and growth difficulties (2). In this article, we will review the epidemiology, clinical manifestations and treatment options; as well as outcomes with surgical and nonsurgical care.

Epidemiology

CPO represents one of the most frequently occurring congenital deformities after clubfoot and cleft lip. The most common syndrome is unilateral cleft lip and palate (46%), followed by CPO (33%). CPO occurs more in females (57%) than in males (43%). Gender differences may be related to differences in timing of embryologic development (3).

Genetics

Cleft lip and palate (CL±P) and cleft palate only (CPO) have different genetic background (4-84). In CPO there is a variety of genes involved in soft palate formation which can be potentially impaired. Consequently several loci carrying transcription and growth factors, their receptors, extracellular matrix components, cell surface adhesion molecules and signalling molecules have been investigated (85-88). The more involved signalling pathways belong to the TGF-β superfamily (TGF-β and BMP genes). In addition half of CPO is associated with a syndromic malformation among them are velo-cardio-facial syndrome, Treacher Collins, Apert and Di George syndrome. Exposures to alcohol, cigarette smoking, steroids, rubella, anticonvulsants (phenobarbital and phenytoin), retinoids, and hypoxia during pregnancy have all been associated with CPO (89). Advanced paternal age, parental folate deficiency, and hypoxia are associated with an increased risk of CPO. If an expecting parent has a cleft palate syndrome the risk of having a child with CPO is 7% (90).

Clinical manifestations

One of the first manifestations associated with CPO is difficulty with feeding. Breast-feeding is possible, in child with CPO, with the use of tools such as a Habermann feeder, Montgomery nipple, bulb syringe, or pigeon feeder. The infant should be fed in a slightly upright position. Aerophagia is a problem in these infants with CPO and breastfeeding may take longer to allow burping. Sometimes, a nasogastric tube or surgical gastric tube may allow child to feed from a bottle (91).
CPO obturator is manufactured to allow separation of the nasal and oropharynx. If velopharyngeal insufficiency is left untreated, or treatment fails, the speech may be incomprehensible. The lack of intraoral breath pressure, in CPO children, may favour difficulties in speaking, particularly consonant weakness, and unintelligible speech. In these cases, the consonant s is very difficult to pronounce. As the child

grows, other sibilants and fricatives become difficult to pronounce. Consonants that are difficult to pronounce are: s, z, d, ch, p, b.
Young children with CPO, who are learning to talk, may substitute some sounds with others. Frequently children with CPO use sounds that require intraoral pressure, instead of nasal consonant (m instead of b). For example, a consonant b is substituted with m. Lack of pronunciations is another form of speech error in which final consonants are deleted as a means of avoiding nasal emission.
Some children with CPO strive to correctly pronounce despite the pressure loss. These children may have weak consonants, but compression may be only slightly impaired. Other modalities to compensate for palate incompetence consist in articulating consonants in a different way. Children with CPO articulate a consonant in pharynx and not in the palate. These individuals have speech distortion, due to pharyngeal fricative and glottal stops. Children with CPO also substitute pharyngeal fricatives for fricative consonants. Hypernasality may provoke errors in pronunciation (perception of excessive nasal resonance during the production of vowels). This distortion is provoked from velopharyngeal incompetence and restriction of the mouth forcing more sound waves into the nasal cavity. During speaking, the palate incompetence of CPO children forces the dorsum tongue in an upper position, resulting in narrowing of the mouth, and an abnormal position of the pharynx and distortion sounds. In addiction, these children with CPO frequently manifest hoarseness, harshness, and vocal nodules. Distortions in speech of CPO children are: low loudness, monotone and strangled voice (92).
Hearing disorders are prevalent among individuals with CPO, as a result of chronic otitis media with effusion due to eustachian tube dysfunction. These children often suffer from conductive hearing loss as a result, and some form of hearing disorder is present in all infants with CPO before the age of 2 years.

Treatment

A multidisciplinary team is mandatory to approach the problems related to CPO. The multidisciplinary team consists of maxillofacial surgeons, audiologists, speech therapists, dentist, orthodontists and prosthodontics. Treatment of CPO has evolved. The techniques of CPO repair, that are practiced today, are the result of principles learned through many years of modifications. The objective of today surgery is to achieve an aesthetic harmony, good oral functionality, optimal speech and a natural growth of the maxilla (93).
Nonsurgical treatment of the CPO consists in performing obturators, which should compensate palatal incompetence. Indications for use of obturators are for those patients who do not want or are too high risk for surgery, those in whom surgery has failed, or patients who would benefit from better alignment of the maxillary segments prior to definitive surgery. The disadvantage in CPO treatment is that the obturator must be relined periodically, and may be irritating to the fragile mucosal surface, difficult to clean, and require cooperation on the child's behalf, and its use is practical beginning at ages 3 to 4 years. The principle advantage of prosthetic devices consists in performing palatal competence, thereby avoiding surgical complications, such as restricted maxillary growth.
CPO patients may achieve normal facial skeleton development. The principal aim of craniofacial surgery is to replace palate competence and to allow normal speech, avoiding surgical complications such as velopharingeal fistulas. The correct timing of surgery must take into account other medical conditions and speech development. Early surgery may have benefits on speech, but may restrict maxilla growth until child has reached 5 years of age. In previous years, restoring surgery of CPO was often delayed until a complete growth of the maxilla or when deciduous molars completed their eruption. Nowadays has been established that the

first outcome is good speech, so surgery may be performed at 10 months of age. Some experts suggest waiting that the child reaches 2 years of age to operate on large CPO. Surgery on soft CPO has been advocated as early as 3 months of age. The Furlow double-opposing Z-plasty and the intravelar veloplasty are the principal techniques for restoring palate incompetence. The Von Langenbeck palatoplasty, the Veau-Wardill- Kilner palatoplasty, or a Bardach two-flap palatoplasty are used for bone restoring. To repair the nasal floor the vomer flaps are used in conjunction with the above hard bone (94).

Outcomes

Palatal fistula, persistent velopharyngeal insufficiency and sleep apnea are considered adverse events after surgery. Fistulas presence may be related to surgeon's ability and type of repair. Wide and bilateral surgical operations may provoke more fistula rates. Speech distortions of CPO are often not evaluated until five to six age, when a child can go to school. Support therapies for children with CPO can be performed for speech therapy, palatoplasty revision, or another compensatory procedure such as a pharyngoplasty or pharyngeal flap. However, velopaharingeal incompetence remains in 5 to 20% of CPO patients, depending on the surgeon's experience and the operative technique utilized. Patients with Pierre Robin more frequently manifest sleep apnea than CPO patients. Careful monitoring of CPO patients is needed to assess for symptoms of sleep apnea. In CPO children, maxillo-facial surgery may be delayed until airway compromise is treated with a tongue-lip adhesion or mandibular distraction. In addiction, CPO children with velocardiofacial syndrome have shown more surgical complications. In CPO children it is due to several factors including poor muscular tone and the anatomic shape of the oropharynx.
The primary goal of surgical therapy is the restore of palatal incompetence and adequate speech development. Optimal management of CPO children consists of a multidisciplinary team and a skilled surgeon (95).

Conclusion

CPO is undoubtedly a complex disease. Fewer analyses of the aetiology of CPO have been performed, but a genetic component also appears important. Genetic and developmental studies about CPO suggest that the formation of the primary palate (lip formation) and the secondary palate (palate formation) follow different mechanisms. Although the two processes are developmentally distinct, similar factors and mechanisms may be involved in the formation of both structures. Different genes may be of functional importance, since processes involve the movement of mesenchymal cells and the closure of two separate regions by either apoptosis of epithelial cells or the transformation of epithelial cells to mesenchymal cells at the point of midline fusion. It is therefore possible, that formation of the primary and secondary palates shares some of the same molecular developmental components. It will be through combining human population studies with developmental biology and molecular genetics that we can achieve a deeper understanding of these processes. Perhaps cleft palate and CPO have distinct etiologies, at least in some cases. Unless future studies separate the two, it will not be possible to discover the different causal pathways. Whenever feasible, future studies should analyse the two separately to explore further the possibility that some factors may affect the risk of one but not the other. Despite CPO can be considered a complex disease to treat, new knowledge and new therapeutic approaches have greatly improved the quality of life of these children. Prenatal diagnosis is an important step in the treatment of this disease.

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